08312293 BIOSIS NO.: 000094074616
EFFECTS OF STAPHYLOCOCCAL ENTEROTOXIN B ON RODENT MAST CELLS
AUTHOR: KOMISAR J; RIVERA J; VEGA A; TSENG J
AUTHOR ADDRESS: DEP. EXPERIMENTAL PATHOL., DIV. PATHOL., WALTER REED ARMY INST. RES., 14TH AND DAHLIA ST. NW., WASHINGTON, D.C. 20307-5100.
JOURNAL: INFECT IMMUN 60 (7). 1992. 2969-2975.
FULL JOURNAL NAME: Infection and Immunity
CODEN: INFIB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Staphylococcal enterotoxin B (SEB) was tested in rodent mast cell cultures for the release of serotonin. Both rat **RBL-2H3** mast cells and murine peritoneal cells released serotonin after SEB stimulation in culture. Release of serotonin in **RBL-2H3** cells depended on the concentration of SEB; an appreciable release was seen at 50 .mu.g/ml. The release of serotonin was not due to cell death. Serotonin release could be enhanced by **bradykinin** but not by vasoactive intestinal peptide, substance P, lipolysaccharide from Salmonella typhimurium, the calcium ionophore A23187, acetylcholine, adenosine, 5-hydroxyeicosatetraenoic acid, indomethacin, or phrobol myristate acetate. SEB bound directly to the membrane of **RBL-2H3** mast cells, and the SEB-binding site, the presumptive receptor, appeared to be a protein. The SEB receptor could not be capped under membrane-capping conditions, and serotonin release could not be enhanced by attempted to cross-link the receptor. These results suggest that mast cells may be an important cell type involved in SEB toxicosis and that release of serotonin maybe enhanced by activation of the kinin-kallikrein system.

DESCRIPTORS: SALMONELLA-TYPHIMURIUM RAT **RBL-2H3** CELLS MURINE CELLS SEROTONIN **BRADYKININ** VASOACTIVE INTESTINAL PEPTIDE SUBSTANCE P LIPOPOLYSACCHARIDE
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
13012 Metabolism-Proteins, Peptides and Amino Acids
15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
17002 Endocrine System-General
22501 Toxicology-General; Methods and Experimental
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
36002 Medical and Clinical Microbiology-Bacteriology
10060 Biochemical Studies-General
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10066 Biochemical Studies-Lipids
10068 Biochemical Studies-Carbohydrates
31000 Physiology and Biochemistry of Bacteria
BIOSYSTEMATIC CODES:
06702 Enterobacteriaceae (1992-)
86375 Muridae
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA):
Microorganisms
Bacteria
Eubacteria
Animals
Chordates
Vertebrates
Nonhuman Vertebrates
Mammals

Nonhuman Mammals
Rodents

5/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07580359 BIOSIS NO.: 000040103523
SUBSTANCE P AND **VIP** INDUCE CONDUCTANCE TRANSIENTS IN **RBL-2H3** A MUCOSAL MAST CELL LINE
AUTHOR: JANISZEWSKI J; BIENENSTOCK J; BLENNERHASSETT M G
AUTHOR ADDRESS: DEP. PATHOL., MCMASTER UNIV., HAMILTON, ONT., CAN. L8N 3Z5.
JOURNAL: THIRTY-FIFTH ANNUAL MEETING OF THE BIOPHYSICAL SOCIETY, SAN FRANCISCO, CALIFORNIA, USA, FEBRUARY 24-28, 1991. BIOPHYS J 59 (2 PART 2). 1991. 224A.
CODEN: BIOJA
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DESCRIPTORS: ABSTRACT VASOACTIVE INTESTINAL POLYPEPTIDE NEUROTRANSMITTER SIGNAL TRANSDUCTION
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
12508 Pathology, General and Miscellaneous-Inflammation and Inflammatory Disease
15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System
20504 Nervous System-Physiology and Biochemistry
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10504 Biophysics-General Biophysical Techniques
32500 Tissue Culture, Apparatus, Methods and Media
BIOSYSTEMATIC CODES:
85150 Vertebrata-Unspecified
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA):
Animals
Chordates
Vertebrates
Nonhuman Vertebrates

5/9/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04528240 BIOSIS NO.: 000029051277
SOMATOSTATIN MODULATION OF MEDIATOR RELEASE BY MOUSE BONE MARROW-DERIVED MAST CELLS RAT SEROSAL MAST CELLS AND RAT BASOPHILIC LEUKEMIA CELLS **RBL-2H3**
AUTHOR: RENOLD F; CHERNOV T; LEE J; PAYAN D G; FURUICHI K; GOETZL E J
AUTHOR ADDRESS: HOWARD HUGHES MED. INST., UNIV. CALIFORNIA, SAN FRANCISCO, CA 94143.
JOURNAL: 69TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ANAHEIM, CALIF., USA, APR. 21-26, 1985. FED PROC 44 (6). 1985. 1917.
CODEN: FEPRA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH
DESCRIPTORS: ABSTRACT HISTAMINE LEUKOTRIENE C-4
CONCEPT CODES:
02506 Cytology and Cytochemistry-Animal
15008 Blood, Blood-Forming Organs and Body Fluids-Lymphatic Tissue and Reticuloendothelial System

17002 Endocrine System-General
17014 Endocrine System-Pituitary
17020 Endocrine System-Neuroendocrinology (1972-)
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
35500 Allergy
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
10066 Biochemical Studies-Lipids
13006 Metabolism-Lipids
13012 Metabolism-Proteins, Peptides and Amino Acids
32500 Tissue Culture, Apparatus, Methods and Media

BIOSYSTEMATIC CODES:
86375 Muridae

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA):
Animals
Chordates
Vertebrates
Nonhuman Vertebrates
Mammals
Nonhuman Mammals
Rodents

5/9/7 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02156968 Genuine Article#: KF375 Number of References: 36
Title: UP-REGULATION OF V(1A) VASOPRESSIN RECEPTORS BY GLUCOCORTICOIDS
Author(s): COLSON P; IBARONDO J; DEVILLIERS G; BALESTRE MN; DUVOID A; GUILLON G
Corporate Source: CNRS,INSERM,CTR PHARMACOL ENDOCRINOL,RUE CARDONILLE/F-34094 MONTPELLIER 05//FRANCE/; CNRS,INSERM,CTR PHARMACOL ENDOCRINOL,RUE CARDONILLE/F-34094 MONTPELLIER 05//FRANCE/; UNIV PAIS VASCO,FAC CIENCIAS,DEPT BIOQUIM & BIOL MOLEC/E-48080 BILBAO//SPAIN/
Journal: AMERICAN JOURNAL OF PHYSIOLOGY, 1992, V263, N6 (DEC), PE1054-E1062
ISSN: 0002-9513
Language: ENGLISH Document Type: ARTICLE
Geographic Location: FRANCE; SPAIN
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: PHYSIOLOGY
Abstract: WRK1 cells (a rat mammary tumor cell line) exhibit a vasopressinergic receptor of V1a subtype tightly coupled to phospholipase C. Addition of dexamethasone to the culture medium principally potentiated the vasopressin-sensitive accumulation of inositol phosphates and to a lesser extent the NaF-sensitive phospholipase C activity. On the opposite, such treatment was without effect on the basal level of intracellular inositol phosphates or on **bradykinin**- or serotonin-sensitive phosphoinositide metabolisms. Glucocorticoid receptors were probably involved in these actions since dexamethasone was found to be more potent than aldosterone or corticosterone. Dexamethasone treatment also increased the number of vasopressin binding sites without affecting its affinity for vasopressin or other specific vasopressin analogues. These results strongly suggest that dexamethasone principally acts at the vasopressin receptor level by affecting its synthesis and/or the translation of its mRNA and also affects the G protein that couples the V1a receptor to the phospholipase C. These results explain how glucocorticoids may regulate the transduction mechanisms involved in vasopressin actions on WRK1 cells. They provide explanations for understanding the cross talk between adrenal steroids and hormones, which mobilize intracellular calcium.
Descriptors--Author Keywords: WRK(1) CELLS ; V(1A) VASOPRESSIN RECEPTOR ; DEXAMETHASONE ; PHOSPHOLIPASE-C
Identifiers--KeyWords Plus: MESSENGER-RNA LEVELS; ACINAR AR42J CELLS;

CALCIUM MOBILIZATION; ADENYLATE-CYCLASE; PHOSPHOLIPASE-C; **RBL-2H3** CELLS; BINDING-SITES; DEXAMETHASONE; STIMULATION; LINE
Research Fronts: 91-0751 001 (CALCITONIN GENE-RELATED PEPTIDE; NEUROGENIC INFLAMMATION IN THE RAT TRACHEA; SENSORY NERVES; PRIMARY AFFERENT NEURONS; AIRWAY **BRADYKININ** RECEPTORS)
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5/9/10 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01261616 Genuine Article#: GJ553 Number of References: 35
Title: EXPRESSION OF AN INWARDLY RECTIFYING K+ CHANNEL FROM RAT BASOPHILIC LEUKEMIA-CELL MESSENGER-RNA IN XENOPUS OOCYTES
Author(s): LEWIS DL; IKEDA SR; ARYEE D; JOHO RH
Corporate Source: MED COLL GEORGIA,DEPT PHARMACOL & TOXICOL/AUGUSTA//GA/30912; BAYLOR COLL MED,DEPT MOLEC PHYSIOL & BIOPHYS/HOUSTON//TX/77030
Journal: FEBS LETTERS, 1991, V290, N1-2, P17-21
Language: ENGLISH Document Type: ARTICLE
Geographic Location: USA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: BIOPHYSICS; BIOCHEMISTRY & MOLECULAR BIOLOGY
Abstract: Rat basophilic leukemia cells (**RBL-2H3**) have previously been shown to contain a single type of voltage-activated channel, namely an inwardly rectifying K+ channel, under normal recording conditions. Thus, **RBL-2H3** cells seemed like a logical source of mRNA for the expression cloning of inwardly rectifying K+ channels. Injection of mRNA isolated from **RBL-**

2H3 cells into Xenopus oocytes resulted in the expression of an inward current which (1) activated at potentials negative to the K+ equilibrium potential (E(K)), (2) decreased in slope conductance near E(K), (3) was dependent on [K+]o and (4) was blocked by external Ba2+ and Cs+. These properties were similar to those of the inwardly rectifying K+ current recorded from **RBL-2H3** cells using whole-cell voltage clamp. Injection of size-fractionated mRNA into Xenopus oocytes revealed that the current was most strongly expressed from the fraction containing mRNA of approximately 4-5 kb. Expression of this channel represents a starting point for the expression cloning of a novel class of K+ channels.

Descriptors--Author Keywords: INWARD RECTIFIER; POTASSIUM CHANNEL; XENOPUS OOCYTE; RNA EXPRESSION

Identifiers--KeyWords Plus: GTP-BINDING PROTEINS; SKELETAL-MUSCLE FIBERS; GUINEA-PIG HEART; POTASSIUM CHANNELS; EGG CELL; ANOMALOUS RECTIFICATION; VENTRICULAR CELLS; STARFISH EGG; PATCH-CLAMP; MEMBRANE

Research Fronts: 89-2063 003 (CALCIUM CHANNELS; SMOOTH-MUSCLE CELLS; ISOLATED RAT HYPOTHALAMIC NEURONS)

89-1447 001 (DEVELOPMENTALLY REGULATED GENE; CAPPING PROTEIN; CDNA SEQUENCE; GENOME ORGANIZATION)

89-4198 001 (NICOTINIC ACETYLCHOLINE-RECEPTOR CHANNELS; SINGLE GUINEA-PIG VENTRICULAR CELLS; GATING MECHANISMS; CARDIAC MYOCYTES)

89-7065 001 (PERTUSSIS TOXIN; MU-TYPE OPIOID RECEPTORS; RAT LOCUS COERULEUS; GTP-BINDING PROTEIN G0 IN NEURONS; CHRONIC **MORPHINE**)

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YATANI A, 1987, V1, P283, MOL ENDOCRINOL

5/9/12 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

02859130 EMBASE No: 1985153089

Somatostatin (SOM 14) modulation of mediator release by mouse bone marrow-derived mast cells (BMMC), rat serosal mast cells (SMC), and rat basophilic leukemia cells (**RBL-2H3**)

Renold F.; Chernov T.; Lee J.; et al.
Howard Hughes Medical Institute, University of California, San Francisco, CA 94143 United States

Federation Proceedings (FED. PROC.) (United States) 1985, 44/6 (No. 8799)
CODEN: FEPRA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

DRUG DESCRIPTORS:
***somatostatin**
interleukin 3; leukotriene c4

MEDICAL DESCRIPTORS:
*basophil; *bone marrow; *leukemia cell; *mast cell
animal cell; nonhuman; mouse; rat; blood and hemopoietic system

CAS REGISTRY NO.: 38916-34-6, 51110-01-1 (**somatostatin**); 72025-60-6 (leukotriene c4)

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029 Clinical and Experimental Biochemistry

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called *secretary component* (Figure 18–19). In secretions, IgA is a dimer. It is transported from the extracellular fluid into the secreted fluid by the same kind of transepithelial transport process (transcytosis) that transfers IgG molecules from maternal blood to fetal blood. In this case the transport is mediated by a special class of Fc receptors that are present on the nonluminal surface of the epithelial cells lining the intestine, bronchi, or th milk, salivary, or tear ducts, where they bin A dimers present in the extracellular fluid (Figure 18–20).

The Fc region of IgE molecules binds with unusually high affinity ($K_a \sim 10^{10}$ liters/mole—see below) to yet another class of Fc receptors. These receptors are located on the surface of *mast cells* in tissues and on *basophils* (see p. 974) in the blood, and the IgE molecules bound to them in turn serve as receptors for antigen. Antigen binding triggers the cells to secrete a variety of biologically active amines (particularly *histamine* and, in some species, *serotonin*) (Figure 18–21). These amines cause dilation and increased permeability of blood vessels and are largely responsible for the clinical manifestations of such *allergic* reactions as hay fever, asthma, and hives. In normal circumstances the blood vessel changes are thought to help white blood cells, antibodies, and complement components to enter sites of inflammation. Mast cells also secrete factors that attract and activate a special class of white blood cells called *eosinophils* (see p. 974), which can kill various types of parasites, especially if the parasites are coated with IgG antibodies.

Antibodies Can Have Either κ or λ Light Chains but Not Both

In addition to the five classes of H chains, higher vertebrates have two types of L chains, κ and λ, either of which may be associated with any of the H chains. An individual antibody molecule always consists of identical L chains and identical H chains; therefore its antigen-binding sites are always identical. This symmetry is crucial for the cross-linking function of secreted antibodies. An Ig molecule, consequently, may have either κ or λ L chains, but never both. No difference in the biological function of these two types of L chain has yet been identified.

The Strength of an Antibody-Antigen Interaction Depends on Both the Affinity and the Number of Binding Sites[16]

The binding of an antigen to antibody, like the binding of a substrate to an enzyme, is reversible. It is mediated by the sum of many relatively weak noncovalent forces, including hydrophobic and hydrogen bonds, van der Waals forces, and ionic interactions. These weak forces are effective only when the antigen molecule is close

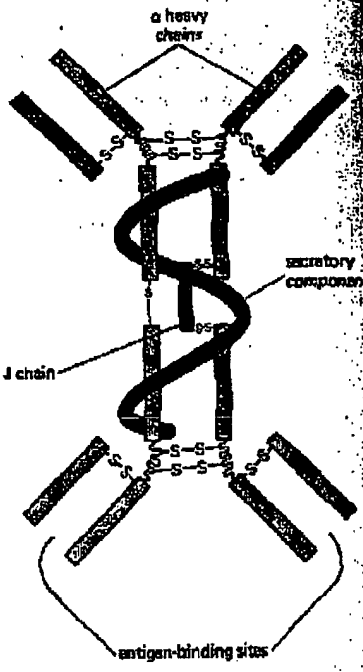

Figure 18–19 A highly schematized diagram of a dimeric IgA molecule found in secretions. In addition to the two IgA monomers that are disulfide-bonded through one of their α heavy chains, there is a single J chain and an additional polypeptide chain of 70,000 daltons called the *secretory component*, which is thought to protect the IgA molecules from being digested by proteolytic enzymes in the secretions.

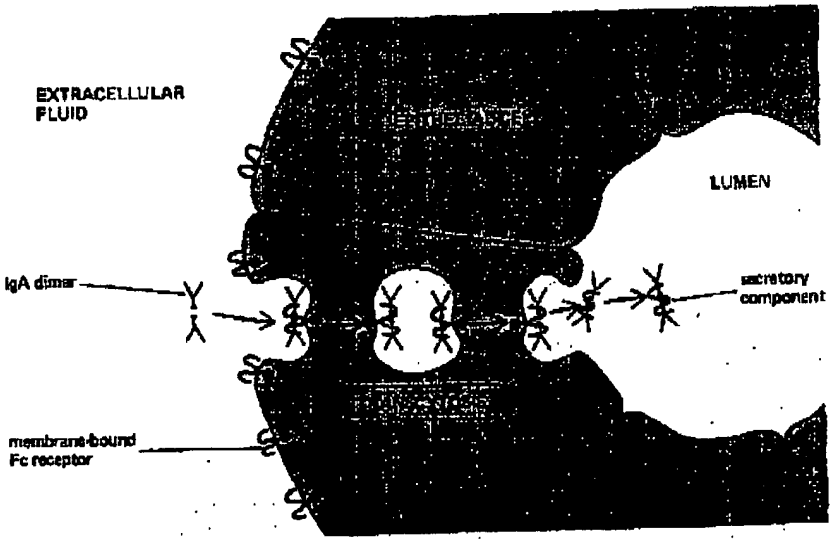

Figure 18–20 The mechanism of transport of a dimeric IgA molecule across an epithelial cell. The IgA binds to a specialized transmembrane Fc receptor protein on the nonluminal surface of the epithelial cell. The receptor-IgA complexes are ingested by receptor-mediated endocytosis, transferred across the epithelial cell cytoplasm in vesicles, and secreted into the lumen on the opposite side of the cell by exocytosis. When exposed to the lumen, the part of the Fc receptor protein that is bound to the IgA dimer (the *secretory component*) is cleaved from its transmembrane tail, thereby releasing the antibody as a complex into the lumen.

The IgA dimers enter the extracellular fluid in secretory organs from two sources. They are produced locally by IgA-secreting plasma cells in these organs, and they are produced in the spleen and lymph nodes, from where they travel in the bloodstream, leaking out of capillaries in various tissues.

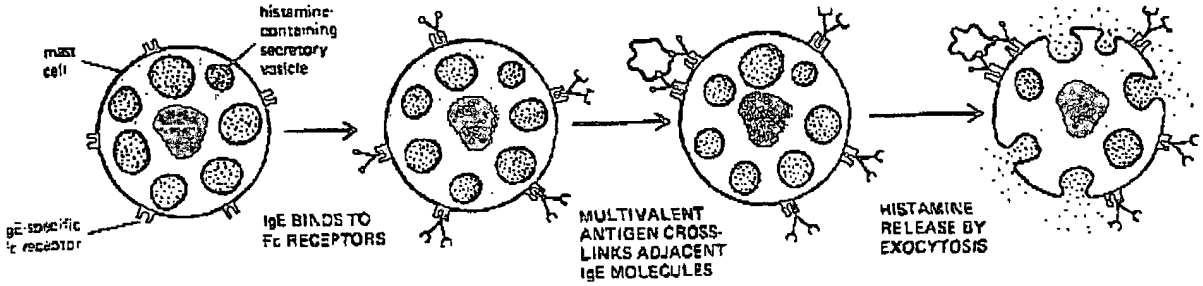

Figure 18–21 Mast cells (and basophils) passively acquire cell-surface receptors that bind antigen. IgE antibodies secreted by active B lymphocytes enter the tissues and bind to Fc receptor proteins on the mast cell surface that specifically recognize the Fc region of these antibodies. Thus, unlike B cells, individual mast cells (and basophils) have cell-surface antibodies with a variety of antigen-binding sites. When an antigen molecule binds to these membrane-bound IgE antibodies so as to cross-link them to their neighbors, it activates the mast cell to release its histamine by exocytosis.

nough to allow some of its atoms to fit into complementary recesses on the urface of the antibody. The complementary regions of a four-chain antibody unit ve its two identical antigen-binding sites; the corresponding region on the antigen s an *antigenic determinant* (Figure 18–22). Most antigenic macromolecules have nany different antigenic determinants; if two or more of them are identical as in a polymer with a repeating structure), the antigen is said to be *multivalent* Figure 18–23).

The reversible binding reaction between an antigen with a single antigenic determinant (denoted Ag) and a single antigen-binding site (denoted Ab) can be expressed as

$$Ag + Ab \rightleftharpoons AgAb$$

The equilibrium point depends both on the concentrations of Ab and Ag and on the strength of their interaction. Clearly, a larger fraction of Ab will become ssociated with Ag as the concentration of Ag is increased. The strength of the interaction is generally expressed as the **affinity constant** (K_a) (see Figure 3–7, p. 84), where

$$K_a = [AgAb]/[Ag][Ab]$$

the square brackets indicate the concentration of each component at equilibrium).

The affinity constant, sometimes called the *association constant*, can be determined by measuring the concentration of free Ag required to fill half of the antigen-binding sites on the antibody. When half the sites are filled, $[AgAb] = [Ab]$ and $K_a = 1/[Ag]$. Thus the reciprocal of the antigen concentration that produces half-maximal binding is equal to the affinity constant of the antibody for the antigen. Common values range from as low as 5×10^4 to as high as 10^{11} liters/mole. The affinity constant at which an immunoglobulin molecule ceases to be considered an antibody for a particular antigen is somewhat arbitrary, but it is unlikely that an antibody with a K_a below 10^4 would be biologically effective; moreover, B cells with receptors that have such a low affinity for an antigen are unlikely to be activated by the antigen.

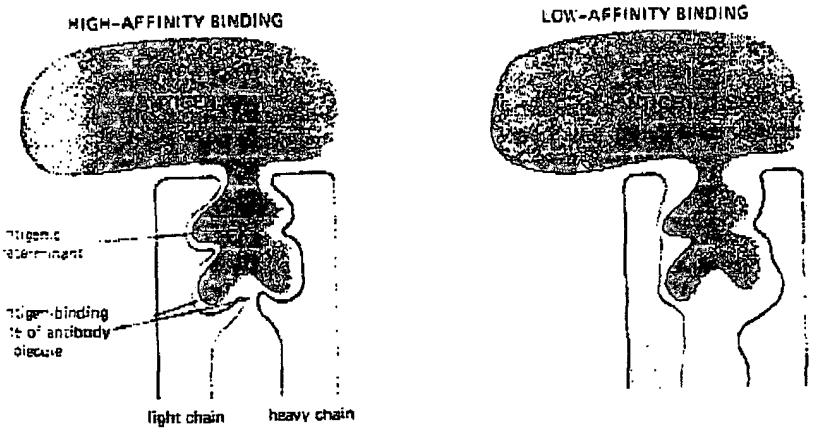

Figure 18–22 Highly schematized diagram of the binding of an antigenic *determinant on a macromolecule* to the antigen-binding site of two different antibody molecules, one of high and one of low affinity. The antigenic determinant is held in the binding site by various weak noncovalent forces. Note that both the light and heavy chains of the antibody molecule usually contribute to *the antigen-binding* site.

All classes of antibody can be made in a membrane-bound form as well as in a soluble, secreted form. The membrane-bound form serves as an antigen receptor on the B cell surface, while the soluble form is made only after the cell is stimulated by antigen to become an antibody-secreting cell. The sole difference between the two forms resides in the carboxyl terminus of the H chain: the H chains of membrane-bound IgM molecules, for example, have a hydrophobic carboxyl terminus, which anchors them in the lipid bilayer of the B cell plasma membrane, whereas those of secreted IgM molecules have instead a hydrophilic carboxyl terminus, which allows them to escape from the cell. Since a B cell contains only one copy of the C_μ gene segment per haploid genome and uses only one of its two H-chain gene pools to make antibodies, its ability to make μ chains with two types of constant regions at first seemed paradoxical. The paradox was resolved with the discovery that the activation of B cells by antigen induces a change in the way μ-chain RNA transcripts are processed in the nucleus, as explained in Figure 18–35 (see also p. 391). The switch from a membrane-bound to a secreted form of the other classes of antibodies involves a similar mechanism.

B Cells Can Switch the Class of Antibody They Make[25]

During B cell development, many B cells switch from making one class of antibody to making another—a process called **class switching**. All B cells begin their antibody-synthesizing lives by making IgM molecules and inserting them into the plasma membrane as receptors for antigen. Before they have interacted with antigen, most B cells then switch and make both IgM and IgD molecules as membrane-bound antigen receptors. Upon stimulation by antigen, some of these cells are activated to secrete IgM antibodies, which dominate the primary antibody response (see p. 1015). Other antigen-stimulated cells switch to making IgG, IgE, or IgA antibodies; memory cells express these molecules on their surface (often simultaneously with IgM molecules), while active B cells secrete them. The IgG, IgE, and IgA molecules are collectively referred to as *secondary* classes of antibodies because they are thought to be produced only after antigen stimulation and because they dominate secondary antibody responses.

Since the class of an antibody is determined by the constant region of its H chain (see p. 1021), the fact that B cells can switch the class of antibody they make without changing the antigen-binding site implies that the same assembled V_H-region coding sequence can sequentially associate with different C_H gene segments. This has important functional implications. It means that in an individual animal a particular antigen-binding site that has been selected by environmental antigens can be distributed among the various classes of immunoglobulin and thereby acquire the different biological properties characteristic of each class.

Class switching occurs by two distinct molecular mechanisms. When virgin B cells change from making membrane-bound IgM alone to the simultaneous production of membrane-bound IgM and IgD, the switch is thought to be due to a change in RNA processing. The cells produce large primary RNA transcripts that contain the assembled V_H-region coding sequence along with both the C_μ and C_δ sequences; IgM and IgD molecules are then produced by differential splicing of these transcripts (Figure 18–36). It is thought that the same mechanism underlies the switch to other classes of membrane-bound Ig when virgin B cells are stimulated by antigen to mature into memory cells that carry IgG, IgE, or IgA as antigen receptors on their surface.

By contrast, terminal maturation to an active B cell secreting one of the secondary classes of antibody is accompanied by an irreversible change at the DNA level—a process called *switch recombination*. It entails deletion of all the C_H gene segments upstream (that is, on the 5′ side as measured on the coding strand) of the particular C_H segment the cell is destined to express (Figure 18–37). Evidence that this step in class switching involves DNA deletion comes from experiments on myeloma cells: myeloma cells that secrete IgG lack the DNA coding for C_μ and C_δ regions, and those that secrete IgA lack the DNA coding for all of the other classes of H-chain C regions.

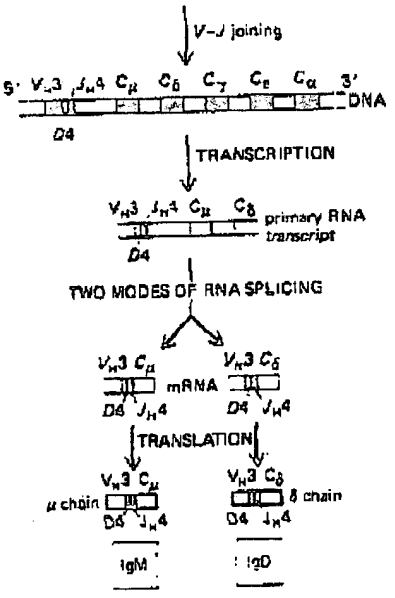

Figure 18–36 B cells that simultaneously make plasma-membrane-bound IgM and IgD molecules having the same antigen-binding sites produce long RNA transcripts that contain both C_μ and C_δ sequences. These transcripts are spliced in two ways to produce mRNA molecules that have the same V_H-region coding sequence joined to either a C_μ or a C_δ sequence. It is possible that the RNA transcripts produced by such cells are even longer than shown and contain all of the various C_H sequences.